

NEW PENDING CLAIM NUMBER	CLAIM RECITATION	SUPPORT IN SPECIFICATION	SUPPORT IN ORIGINAL CLAIMS (If Applicable)
283 (composition)	<p>a first part . . . molecular bridging entity comprising a first portion . . . and a second portion comprising . . . nucleic acid sequences or segments comprising one or more nucleic acid sequences or segments</p> <p>a second part which comprises more than one signalling entity, each such entity comprising a nucleic acid portion . . . and</p> <p>one or more signal generating portions capable of providing a detectable signal.</p>	<p>Page 7, last ¶ ("providing a molecular bridging entity (B) having thereon (i) . . . and (ii)")</p> <p>Page 8, penultimate ¶ ("The invention provides . . . various elements and components to be used therein, such as various molecular bridging entities. . . .")</p> <p>Page 13, 2nd full ¶ (for "molecular bridging entity")</p> <p>Page 16, 1st ¶ (" . . . many more polynucleotide sequence portions than recognizing portions, or vice versa.")</p> <p>Page 22, 1st ¶ (" . . . ratio of polynucleotide portions to recognizing portions on the bridging entity is greater than 1")</p> <p>Page 22, 1st ¶ (" . . . ratio of polynucleotide portions to recognizing portions on the bridging entity is greater than 1")</p> <p>[Note: This is support for "more than one signalling entity . . ."]</p> <p>Page 22, 1st ¶ ("When the ratio of signal generating portion . . . is greater than 1 . . .")</p> <p>Page 8, lines 12-13 ("detecting a signal by means of said signal generating portion present in said complex.")</p>	<p>Claim 100 ("A kit . . . comprising . . . (II) . . . a molecular bridging entity (B) having thereon: . . . (i) a portion capable of recognizing said . . . analyte (A); and (ii) a portion comprising a polynucleotide sequence: . . .")</p> <p>Claim 20 ("said polynucleotide sequence in said bridging entity is covalently attached to another polynucleotide sequence")</p> <p>Claim 100 ("A kit . . . comprising: . . . (III) a second container means containing a signalling entity (C) . . .")</p> <p>Claim 1, last step ("detecting a signal by means of said signal generating portions present in said complex") is support for "capable of providing a detectable signal")</p> <p>Claim 1 (preamble "detecting in a sample an analyte (A) having a molecularly recognizable portion thereon")</p> <p>Claim 1 (preamble "detecting in a sample an analyte (A) having a molecularly recognizable portion thereon")</p> <p>Claim 20 (same as Claim 283 above)</p> <p>Claim 1 ("detecting a signal . . . " is support for "capable of providing a detectable signal") (same as Claim 283 above)</p>
284 (composition)	<p>a first part which comprises an analyte having one or more molecularly recognizable portions thereon</p> <p>a second part which comprises a molecular bridging entity comprising a first portion . . . and a second portion comprising one or more nucleic acid sequences or segments</p> <p>a third part which comprises more than one signalling entity, each such entity comprising a nucleic acid portion . . . and one or more signal generating portions . . . signal.</p>	<p>Page 7 (2nd full ¶) (the analyte is present in the sample)</p> <p>Page 10, lines 3-10 (lines 3-6 in particular) ("When analyte is present in the sample being analyzed . . .")</p> <p>Page 11, 1st full ¶ ("The term 'analyte' . . . includes any substances or substances either alone or in admixtures . . .")</p> <p>Page 7, last ¶ (see Claim 283 above)</p> <p>Page 8, penultimate ¶ (see Claim 283 above)</p> <p>Page 13, 2nd full ¶ (see Claim 283 above)</p> <p>Page 16, 1st ¶ (see Claim 283 above)</p> <p>Page 22, 1st ¶ (see Claim 283 above)</p> <p>Page 22, 1st ¶ (see Claim 283 above)</p>	

285 (composition)	a complex which comprises a molecular bridging entity comprising a first portion . . . and a second portion comprising one or more nucleic acid sequences or segments and more than one signalling entity, each such entity comprising a nucleic acid portion . . . and one or more signal generating portions capable of providing a detectable signal.	Page 8, lines 4-11 ("forming a complex . . .") Page 10, lines 3-10 ("The complex formed thereby . . .") Page 28, 1st ¶ (" . . . to allow complexation . . .") Page 61, No. 15 ("The (G+) and derivatized (G-) DNAs are mixed in equimolar concentration and allowed to hybridize to target DNAs and to each other") Figure 1 ("Single Step or Multi-Step") Page 16, 1st ¶ (see Claim 283 above) Page 22, 1st ¶ (see Claim 283 above) Page 22, 1st ¶ (see Claim 283 above)	Claim 1, first step ("providing a molecular bridging entity (B) and (C) a signalling entity . . ." and second step ("forming a complex . . .")
286 (composition)	a complex which comprises: an analyte having one or more molecularly recognizable portions thereon a molecular bridging entity comprising a first portion . . . and a second portion	Page 8, lines 4-11 Page 10, lines 3-10 Page 28, 1st full ¶ (" . . . analyte is incubated with molecular bridging entity to allow complexation . . .") Page 8, lines 4-11 (re: complex) Page 10, lines 3-10 (re: complex) Page 28, 1st full ¶ (re: complex) more than one signalling entity, each such entity comprising a nucleic acid portion . . . and one or more signal generating portions capable of providing a detectable signal,	Claim 1, last step ("forming a complex comprising (1) said analyte (A) complexed . . . to (2) said recognizing portion of said entity (B) complexed . . . to (3) said polynucleotide portion of said signalling entity (C) . . .") Claim 20 (same as Claim 283 above) Claim 1 ("detecting a signal . . ." is support for "capable of providing a detectable signal") (same as Claim 283 above)

287 (composition)	a first part which comprises more than one molecular bridging entity, each such entity comprising a first portion . . . and a second portion . . . a second part which comprises more than one signalling entity, each such entity comprising a nucleic acid portion . . . and one or more signal generating portions . . .	Page 8, penultimate ¶ (for example, "various molecular bridging entities . . ."), through Page 9, 1st ¶ (for example, "multi-component assay system") Page 15, 1st ¶ ("It is thus preferred to choose polynucleotide sequence portions on the bridging entity . . .") Page 16, 1st ¶ (The molecular ratio of the recognizing portion on the bridging entity, to the polynucleotide sequence portion thereon need not necessarily be 1:1. There may be many more polynucleotide sequence portions than recognizing portions, or vice versa.") Page 22, 1st ¶ (see Claim 283 above)	Claim 100 (see Claim 283 above)
288 (composition)	a first part which comprises an analyte . . . a second part which comprises more than one molecular bridging entity . . . a third part which comprises more than one signalling entity . . .	Page 7 (second full ¶) (the analyte is present in the sample) Page 10, lines 3-10 (3-6 in particular) ("When analyte is present in the sample being analyzed . . .") Page 11, 1st full ¶ ("The term 'analyte' . . . includes any substances or substances either alone or in admixtures . . .") Page 8, penultimate ¶ (see Claim 287 above) Page 15, 1st ¶ (see Claim 287 above) Page 16, 1st ¶ (see Claim 287 above) Page 22, 1st ¶ (see Claim 283 above)	Claim 1 (see Claim 284 above) Claim 100 (see Claim 283 above)
289 (composition)	a complex which comprises more than one molecular bridging entity . . . and more than one signalling entity	Page 8, lines 4-11; Page 10, lines 3-10; Page 28, 1st ¶; Page 61, No. 15 and Figure 1 (for "complex," see Claim 285 above) Page 8, penultimate ¶ (see Claim 287 above) Page 15, 1st ¶ (see Claim 287 above) Page 16, 1st ¶ (see Claim 287 above) Page 8, lines 4-11 & Page 10, lines 3-11 (re: complex) Page 22, 1st ¶ (see Claim 283 above for more than one signalling entity and "more than one signal generating	Claim 1 (see Claim 285 above) Claim 1 (see Claim 283 above)

		portions")	
290 (composition)	a complex which comprises an analyte . . . more than one molecular bridging entity . . . more than one signalling entity . . .	Page 8, lines 4-11 Page 10, lines 3-10 Page 28, 1st full ¶ (see Claim 286 above) Page 8, penultimate ¶ (see Claim 287 above) Page 15, 1st ¶ (see Claim 287 above) Page 16, 1st ¶ (see Claim 287 above) Page 8, lines 4-11 & Page 10, lines 3-11 (re: complex) Page 22, 1st ¶ (see Claim 283 above for "more than one signalling entity" and "more than one signal generating portions")	Claim 1 (see Claim 286 above)
291 (composition)	a first part which comprises a molecular bridging entity . . . and a second part which comprises more than one signalling entity, each such entity comprising a nucleic acid portion . . . and one or more polynucleotides which have been chemically modified or artificially altered.	Page 7, last ¶ (see Claim 283 above) Page 8, penultimate ¶ (see Claim 283 above) Page 13, 2nd full ¶ (see Claim 283 above) Page 16, 1st ¶ (see Claim 283 above) Page 22, 1st ¶ (see Claim 283 above) Page 22, 1st ¶ (see Claim 283 above)	Claim 100 (see Claim 283 above) Claim 38 ("wherein said signalling entity is a polynucleotide Polymer"); Claim 39 ("wherein said polynucleotide polymer is a naturally occurring modified DNA"); and Claim 42 ("wherein said modified DNA carries a cloned insert.")
292 (composition)	a complex which comprises a molecular bridging entity . . . and more than one signalling entity, each such entity comprising a nucleic acid portion . . . and one or more polynucleotides which have been chemically modified or artificially altered.	Page 8, lines 4-11; Page 10, lines 3-10; and Page 28, 1st full ¶ (re: complex and molecular bridging entity) Page 8, lines 4-11 & Page 10, lines 3-11 (re: complex) Page 22, 1st ¶ (see Claim 283 above for "more than one signalling entity" and "more than one signal generating portions")	Claim 1 (see Claim 283 above) Claim 38 ("wherein said signalling entity is a polynucleotide polymer"); Claim 39 ("wherein said polynucleotide polymer is a naturally occurring modified DNA"); and Claim 42 ("wherein")

		said modified DNA carries a cloned insert."
293 (composition)	a first part which comprises an analyte . . . a second part which comprises a molecular bridging entity . . . and	Page 7, 2nd full ¶; Page 10, lines 3-10; and Page 11, 1st full ¶ (see Claim 284 above)
	Page 7, last ¶ (see Claim 283 above) Page 8, penultimate ¶ (see Claim 283 above) Page 13, 2nd full ¶ (see Claim 283 above) Page 16, 1st ¶ (see Claim 283 above) Page 22, 1st ¶ (see Claim 283 above) a third part which comprises more than one signalling entity, each such entity comprising a nucleic acid portion . . . and	Claim 38 ("wherein said signalling entity is a polynucleotide polymer"); Claim 39 ("wherein said polynucleotide polymer is a naturally occurring modified DNA"); and Claim 42 ("wherein said modified DNA carries a cloned insert.")
294 (composition)	one or more polynucleotides which have been chemically modified or artificially altered. a complex which comprises an analyte . . . a molecular bridging entity . . . and	Page 19, last ¶, through Page 21, line 10 (see in particular Page 20, last ¶, through Page 21, line 6) Page 8, lines 4-11; Page 10, lines 3-10; and Page 28, 1st full ¶ (see Claim 286 above)
	more than one signalling entity, each such entity comprising a nucleic acid portion . . . and	Page 8, lines 4-11; and Page 10, lines 3-11 (re: complex) Page 22, 1st ¶ (see Claim 283 above for "more than one signalling entity" and "more than one signal generating portions")
	one or more polynucleotides which have been chemically modified or artificially altered.	Page 19, last ¶, through Page 21, line 10 (see in particular Page 20, last ¶, through Page 21, line 6)
295 (composition)	. . . wherein said analyte comprises a biological system.	Claim 38 ("wherein said signalling entity is a polynucleotide polymer"); Claim 39 ("wherein said polynucleotide polymer is a naturally occurring modified DNA"); and Claim 42 ("wherein said modified DNA carries a cloned insert.")
296 (composition)	wherein said biological system comprises at least one member selected from . . . a virus or a viral component thereof, and a cell or a cellular component thereof.	Claim 6 ("wherein said analyte is selected from . . . a virus, a viral component, . . . a cell, a cellular component, . . .")

297 (composition)	wherein said cell or component thereof comprises a bacterium or a bacterial component thereof.	Page 11, 7th line from bottom of page ("bacteria of various different types") Page 11, last two lines, through Page 12, line 2 ("Bacteria, either whole or fragments thereof, such as cell walls or other recognizable portions, include both gram positive and gram negative bacteria.") Page 23, lines 8-9 ("insoluble phases such as bacterial particles.")	Claim 6 ("wherein said analyte is selected from . . . a bacterium, a bacterial component, . . .") Claim 84 ("wherein said prokaryotic cell is a bacterium.")
298 (composition)	wherein said biological system comprises a pathogen or a component thereof.	Page 31, 2nd full ¶ (" . . . a method of detecting antibodies against certain infectious diseases in animals . . .") Page 60, No. 13 (" . . . by inserting sequences from a variety of pathogens . . .")	Claim 6 ("wherein said analyte is selected from . . . any pathogenic or non-pathogenic component of a sample . . .")
299 (composition)	wherein said analyte is selected from . . . a nucleic acid and a protein.	Page 11, lines 14-17 ("Among the common analytes are proteins, . . . protein complexes, nucleic acids or segments thereof.")	Claim 3 ("wherein said analyte is proteinaceous.") Claim 4 ("wherein the molecularly recognizable portion on said analyte comprises nucleic acid.")
300 (composition)	wherein said nucleic acid is selected from . . . an oligo- or polyribonucleotide, an oligo- or polydeoxyribonucleotide, a polypurine, a poly-pyrimidine and an analog-containing polymer . . .	Page 11, lines 16-17 ("nucleic acids or segments thereof") Page 12, lines 13-16 ("A molecularly recognizable portion on an analyte may be, for example, a polynucleotide sequence, such as RNA or DNA, to be recognized by its complementary sequence . . .") Page 13, 1st full ¶ ("Among the most common recognizable portions are . . . the nucleic acid sequences present in the DNA or RNA of organisms . . .") Page 15, last ¶ ("By 'polynucleotide' is meant to include both polynucleotides, polydeoxyribonucleotides, or any poly-purine, -pyrimidine or analog and combinations thereof.")	Claim 4 (see Claim 299 above) Claims 69 and 147 ("wherein said recognizable portion on said analyte is a polynucleotide sequence.") Claim 78 ("A DNA molecule carrying a polynucleotide portion which comprises a sequence selected from . . . poly dGT, poly dAC, poly dCT, poly dAT, poly dGA, poly dGC, poly dG, poly dC, poly dT, poly dA, . . .") Claims 81 and 92 ("wherein said sequence is at least an oligonucleotide . . .")
301 (composition)	wherein said molecular bridging recognizing first portion comprises a low molecular weight organic compound.	Page 15, last ¶ ("small molecular weight organic compounds with polynucleotides") Page 23, lines 7-8 ("4) small molecular weight compounds (e.g., MW less than about 1000)")	

302 (composition)	wherein said molecular bridging recognizing first portion is selected from . . . an antigen and an antibody.	<p>Page 12, 2nd ¶ (" . . . an antigen portion, to be recognized by its corresponding monoclonal or polyclonal antibody; an antibody portion, to be recognized by its corresponding antigen.")</p> <p>Page 13, 2nd full ¶ ("These two portions of the bridging entity may be of the same type . . . or of a different type (one being, for example, an antibody portion and the other the polynucleotide portion.)")</p> <p>Page 14, 1st ¶ ("If the molecularly recognizable portion on the analyte is a generalized antigen, the recognizing portion on the bridging entity should be an antibody thereto.")</p> <p>Page 15, 2nd ¶ ("Specific examples of bridging entities . . . are covalently attached entities of monoclonal or polyclonal antibodies, . . . protein antigens with polynucleotides . . .")</p> <p>Page 31, 1st full ¶ ("Another use comprises . . . detecting . . . the presence of cancer associated antigens such as CEA . . .")</p> <p>Page 31, 2nd full ¶ ("Another use includes a method of detecting antibodies against certain infectious diseases in animals, by using antigen therefor as a recognizing portion in the molecular bridging entity.")</p> <p>Page 48, Example 15 ("Synthesis of DNA-Ig G Conjugates")</p>	<p>Claims 8 and 103 ("wherein said recognizing portion on said bridging entity comprises an antigen.")</p> <p>Claims 9 and 104 ("wherein said recognizing portion on said bridging entity comprises an antibody.")</p> <p>Claims 21 and 116 ("wherein said polynucleotide sequence in said bridging entity is covalently attached to an antibody.")</p> <p>Claims 22 and 117 ("wherein said polynucleotide sequence in said bridging entity is covalently attached to an antigen.")</p> <p>Claim 72 ("A polynucleotide sequence covalently attached to an antibody.")</p>
303 (composition)	wherein said antibody comprises a polyclonal or a monoclonal antibody.	<p>Page 12, 2nd ¶ ("A molecularly recognizable portion on an analyte may be . . . an antigen portion, to be recognized by its corresponding monoclonal or polyclonal antibody.")</p> <p>Page 15, 2nd ¶ ("Specific examples of bridging entities . . . are covalently attached entities of monoclonal or polyclonal antibodies with polynucleotides.")</p>	<p>Claim 73 ("wherein said antibody is monoclonal.")</p>
304 (composition)	wherein said molecular bridging recognizing first portion is selected from . . . a saccharide and a lectin.	<p>Page 12, 2nd ¶ ("A molecularly recognizable portion on an analyte may be . . . a lectin portion, to be recognized by its sugar; a sugar portion, to be recognized by its lectin.")</p> <p>Page 14, 1st ¶ ("The same is true with respect to the complementary pairs sugar/lectin.")</p> <p>Page 15, 2nd ¶ ("Specific examples of bridging entities . . . are covalently attached entities of . . . lectins with polynucleotides.")</p> <p>Page 23, 1st ¶ ("covalent attachment of polynucleotides, or individual components thereof, to . . . 2) saccharide moieties.")</p> <p>Page 25, 1st full ¶ ("The attachment of polynucleotide sequences to saccharides can be carried out . . .")</p>	<p>Claims 10 and 105 ("wherein said recognizing portion on said bridging entity comprises a saccharide.")</p> <p>Claims 11 and 106 ("wherein said recognizing portion on said bridging entity comprises a lectin.")</p> <p>Claims 23 and 118 ("wherein said polynucleotide sequence in said bridging entity is covalently attached to a saccharide")</p> <p>Claims 24 and 119 ("wherein said polynucleotide sequence in said bridging entity is covalently attached to a lectin")</p> <p>Claim 74 ("A polynucleotide sequence covalently attached to a lectin.")</p> <p>Claim 75 ("A polynucleotide sequence covalently attached to a saccharide having up to 20 saccharide units.")</p>

305 (composition)	wherein said molecular bridging recognizing first portion is selected from . . . a hormone and a receptor therefor.	Page 12, 2nd ¶ ("A molecularly recognizable portion on an analyte may be . . . a hormone portion, to be recognized by its receptor; a receptor portion, to be recognized by its hormone.") Page 14, 1st ¶ ("The same is true with respect to the complementary pairs . . . receptor/hormone.") Page 15, 2nd ¶ ("Specific examples of bridging entities . . . are covalently attached entities of . . . receptors with polynucleotides, hormones with polynucleotides.") Page 30, last ¶, through Page 31, line 1 ("Another use includes . . . identifying or locating hormone receptor sites on the surface of cells, which comprises binding a hormone receptor binding compound present in the bridging entity to the receptor site . . .") Claim 77 ("A polynucleotide sequence covalently attached to a hormone.")	Claims 12 and 107 ("wherein said recognizing portion on said bridging entity comprises a hormone.") Claims 13 and 108 ("wherein said recognizing portion on said bridging entity comprises a hormone.") Claim 15 ("wherein said recognizing portion on said bridging entity comprises . . . a receptor protein") Claims 25 and 120 ("wherein said polynucleotide sequence in said bridging entity is covalently attached to a hormone.") Claims 26 and 121 ("wherein said polynucleotide sequence in said bridging entity is covalently attached to a receptor") Claim 76 ("A polynucleotide sequence covalently attached to a receptor.") Claim 77 ("A polynucleotide sequence covalently attached to a hormone.")
306 (composition)	wherein said molecular bridging entity recognizing first portion is selected from . . . an enzyme, an allosteric effector, an enzyme substrate and an enzyme cofactor.	Page 12, 3rd line from bottom of page, through Page 13, line 2 ("an inhibitor portion, to be recognized by its enzyme; an enzyme portion, to be recognized by a cofactor enzyme binding site; a cofactor enzyme binding site portion, to be recognized by its cofactor;") Page 14, lines 5-6 ("complementary pairs . . . inhibitor/enzyme") Page 15, full ¶ ("Specific examples of bridging entities . . . enzyme inhibitors with polynucleotides, enzyme cofactors with polynucleotides, and combinations and permutations thereof.")	Claims 14 and 109 ("wherein said recognizing portion on said bridging entity comprises an enzyme inhibitor or enzyme cofactor") Claim 15 ("wherein said recognizing portion on said bridging entity comprises an enzyme active site, a cofactor binding site . . .") Claims 27 and 122 ("wherein said polynucleotide sequence in said bridging entity is covalently attached to an enzyme inhibitor or enzyme cofactor") Claims 28 and 123 ("wherein said polynucleotide sequence in said bridging entity is covalently attached to an enzyme") Claim 110 ("wherein said recognizing portion on said bridging entity comprises an enzyme active site or cofactor binding site.")
307 (composition)	wherein said molecular bridging recognizing first portion is selected from . . . a ligand and a receptor therefor.	Page 13, lines 2-4 ("binding ligand recognized by its substrate and vice versa (i.e. biotin-avidin); or any permutation or combinations thereof.")	

308 (composition)	wherein said molecular bridging recognizing first portion is selected from . . . a protein and a protein receptor thereafter.	<p>Page 13, 1st full ¶ ("Among the most common molecularly recognizable portions are the three-dimensional protein structures present in antigens of various different sorts, the cell wall structures present in various cells . . .")</p> <p>Page 15, full ¶ ("Specific examples of bridging entities . . . protein antigens with polynucleotides . . .")</p> <p>Page 23, lines 2-4 ("method of preparation . . . will relate to the covalent attachment of polynucleotides, or individual components thereof, to 1) protein moieties;")</p> <p>Page 23, 2nd ¶ ("The covalent attachment of polynucleotide sequences to proteins . . .")</p> <p>Page 34, last five lines ("1) Chemical activation of oligonucleotides for subsequent coupling to proteins . . . and "2) Chemical activation of proteins for . . . coupling to DNA.")</p> <p>Page 35, lines 6-7 ("5) Coupling of DNA to protein.")</p> <p>Page 36, lines 8-10 ("5) Coupling of DNA to protein. . . . A. to protein. Examples 15, 19, 20.</p>
309 (composition)	wherein said molecular bridging recognizing first portion comprises a nucleic acid	<p>Page 11, 2nd ¶ ("Among . . . are . . . nucleic acids or segments thereof . . . and "Among the most common nucleic acids . . .")</p>
310 (composition)	wherein said nucleic acid comprises an oligo- or polynucleotide.	<p>Claims 7 and 102 ("wherein said recognizing portion on said bridging entity comprises a polynucleotide sequence.")</p> <p>Claim 69 (" . . . said recognizing portion on said bridging entity is a polynucleotide sequence . . .")</p> <p>Page 12, 2nd ¶ (" . . . a polynucleotide sequence . . . to be recognized by its complementary sequence.")</p> <p>Page 13, 2nd full ¶ ("These two portions of the bridging entity may be of the same type (i.e., both of them polynucleotide sequences, albeit different ones)")</p> <p>Page 13, 2nd line from bottom of page, through Page 14, line 1 (" . . . the recognizing portion of the bridging entity should be a complementary polynucleotide sequence or 'probe' ")</p> <p>Page 15, full ¶ ("Specific examples of . . . polynucleotides with polynucleotides, . . . receptors with polynucleotides, . . .")</p> <p>Page 23, lines 4-6 ("covalent attachment of polynucleotides. . . to . . . 3) other polynucleotide moieties.")</p> <p>Page 25, last 2 ¶s ("The attachment of polynucleotide sequences to other polynucleotide sequences . . . and "Other methods for attaching polynucleotides to polynucleotides . . .")</p> <p>Page 30, 2nd and 3rd full ¶s (" . . . diagnose genetic disorders by preparing a polynucleotide complementary to a DNA gene sequence . . . and "Another use . . . chromosomal karyotyping . . . using a series of modified polynucleotides . . .")</p>

311 (composition)	wherein said oligo- or polynucleotide comprises a modified oligo- or polynucleotide.	Page 18, 1st ¶ ("The polynucleotide portion on the signalling entity is defined by the same parameters as the complementary portion on the molecular bridging entity . . .") Page 20, last ¶, through Page 21, 1st ¶ ("A thorough description of various non-radioactive signal generating systems, both biotin/avidin-based and non-biotin/avidin-based can be found . . . fully incorporated by reference.") Page 21, 2nd ¶ (" . . . need not be a polynucleotide which has been chemically modified or artificially altered in any way . . .")	Claim 39 ("wherein said polynucleotide polymer is a naturally occurring modified DNA.")
312 (composition)	wherein said modified oligo- or polynucleotide comprises one or more nucleotides modified on the sugar, phosphate, base, or combinations thereof	Page 20, last ¶, through Page 21, 1st ¶ ("A thorough description of various non-radioactive signal generating systems, both biotin/avidin-based and non-biotin/avidin-based can be found . . .") (See Claim 311 above)	Claim 30 ("wherein said DNA is single-stranded.") Claim 43 ("wherein said polymer is single-stranded.")
313 (composition)	wherein said oligo- or polynucleotide is single-stranded or partially double-stranded.	Page 10, 2nd ¶ ("Bridging entity 11, shown as a single-stranded circular polynucleotide polymer . . .") Page 11, 2nd ¶ ("nucleic acids or segments thereof, either single- or double-stranded.") Page 16, 2nd ¶ ("Among preferred bridging entities . . . are circular polymers of single- or double-stranded DNA . . .") Page 17, 1st full ¶ ("ideally, a single-stranded DNA polymer can be provided . . .") Pages 57-61 (Example 32)	Claims 29 and 124 ("wherein said bridging entity is a circular DNA polymer.")
314 (composition)	wherein said oligo- or polynucleotide is circular or linear.	Page 10, 2nd ¶ ("Bridging entity 11, shown as a single-stranded circular polynucleotide polymer.") Page 11, 2nd ¶ ("nucleic acids or segments thereof, either single- or double-stranded.") Page 16 ("Among preferred bridging entities . . . are circular polymers of single- or double-stranded DNA . . .")	Claims 29 and 124 ("wherein said bridging entity is a circular DNA polymer.")
315 (composition)	wherein said oligo- or polynucleotide is selected from . . . an oligo- or polynucleotide, an oligo- or polydeoxyribonucleotide, a poly-pyrimidine or analog, a poly-purine, a poly-pyrimidine and an analog-containing polymer . . .	Page 15, 1st ¶ ("By 'polynucleotide' is meant to include both polynucleotides, polydeoxyribonucleotides, or any poly-purine, pyrimidine or analog and combinations thereof.")	Claim 18 ("wherein said polynucleotide sequence on said bridging entity comprises a poly deoxy G, poly deoxy C, poly deoxy T or poly deoxy A sequence, or any poly-ribo or -deoxyribo purine, pyrimidine or analog or analog . . .")

316 (composition)	wherein said nucleic acid sequences or segment in the molecular bridging entity second portion comprises an oligo- or polynucleotide.	Page 7, 6th and 7th lines from bottom of page ("ii) a portion comprising a polynucleotide sequence.") Page 9, 4th and 5th lines from bottom of page ("Bridging entity 3, in addition, carries a portion 5 comprising a polynucleotide sequence.") Page 14, 1st full ¶ ("The second portion of the molecular bridging entity must comprise a polynucleotide sequence.") Page 33 ("the kit carrier contains a first container means comprising a bridging system which is DNA carrying a polynucleotide portion of predetermined sequence . . .")	Claim 1 ("providing a molecular bridging entity (B) having thereon . . . (ii) a portion comprising a polynucleotide sequence;") Claim 100 ("A kit . . . comprising . . . (ii) a first container means containing a molecular bridging entity (B) having thereon . . . (ii) a portion comprising a polynucleotide sequence;")
317 (composition)	wherein said oligo- or polynucleotide comprises a modified oligo- or polynucleotide.	See Claim 311 above.	See Claim 311 above.
318 (composition)	wherein said modified oligo- or polynucleotide comprises one or more nucleotides modified on the sugar, phosphate, base or combination thereof.	See Claim 312 above.	See Claim 312 above.
319 (composition)	wherein said nucleic acid sequences or segments in the molecular bridging entity second portion is single-stranded or partially double-stranded.	See Claim 313 above.	See Claim 313 above.
320 (composition)	wherein said nucleic acid sequences or segments in the molecular bridging entity second portion is linear or circular	See Claim 314 above.	See Claim 314 above.
321 (composition)	wherein said oligo- or polynucleotide is selected from . . . an oligo- or polyribonucleotide, an oligo- or polydeoxyribonucleotide, a poly-purine, a poly-pyrimidine and an analog-containing polymer . . .	See Claim 315 above.	See Claim 315 above.

322 (composition)	wherein said nucleic acid sequences or segments in the molecular bridging entity second portion is derived from a phage selected from . . . a T even phage, a filamentous phage, an M13 phage, or an M13 variant.	Page 16, 2nd ¶ ("Among preferred bridging entities . . . are circular polymers . . . The single-stranded one include so-called filamentous phages, such as fd, f1 and M13 . . .") Page 18, 1st ¶ ("The polynucleotide portion on the signalling entity is defined by the same parameters as the complementary portion on the molecular bridging entity . . .") Page 21, 2nd ¶ ("Some biological systems perform <u>in vivo</u> modifications which can be utilized . . . One such system is the phage T4 . . . Other T (even) phages such as T2, T6, or T8 can also be used.") Pages 57-59, Example 32 Use of Bacteriophage M13 as Bridging Entity	Claims 30 and 126 ("wherein said circular DNA polymer is derived from a filamentous phage.") Claims 31 and 127 ("wherein said filamentous phage is M13 or a variant thereof.") Claims 32 and 128 ("wherein said M13 phage carries a sequence portion . . .") Claim 40 ("wherein said polynucleotide polymer is derived from a T (even) phage.") Claim 41 ("wherein said T (even) phage phage is T4.") Claim 44 ("wherein said polymer is derived from a filamentous phage.") Claim 45 ("wherein said phage is M13 or a variant thereof") Claim 67 ("wherein said modified DNA is derived from a T4 phage.") Claim 70 ("wherein said bridging entity is derived from a filamentous phage.") Claim 71 ("wherein said signalling entity is derived from a filamentous phage.") Claim 36 ("wherein said polynucleotide portion on said signalling entity comprises . . . a repeating sequence of low complexity") Claim 78 ("a polynucleotide portion which comprises a sequence selected from . . . a repeating low-complexity polynucleotide.")
323 (composition)	wherein said molecular bridging entity second portion comprises a nucleic acid sequence or segment of repeating low complexity.	Page 15, 1st ¶ ("or any other low complexity (repeating) sequence.")	Page 15, 1st ¶ ("sequences comprising poly deoxy G, poly deoxy A, poly deoxy GT, poly deoxy GA, poly deoxy GAT, poly deoxy GTA, or any other low complexity (repeating) sequence.") Page 17, 1st full ¶ ("a poly G, or poly GT, or poly dG, or poly dC, or poly dCA, or poly dGdT, polynucleotide portion.") Page 27, 1st ¶ ("If the polynucleotide sequence comprises a strand of any one nucleotide (e.g., poly dG or poly dC) or a strand of any dinucleotide pair (e.g., poly dGT, or the like), the same can be readily prepared . . .") Page 38, ("4. The ligation products are isolated. They are double-stranded poly d (G-T) poly d (A-C).")

325 (composition)	wherein said molecular bridging entity first portion and said molecular bridging entity nucleic acid second portion are incapable of hybridizing to identical oligo- or polynucleotide sequences.	Page 14 ("The second portion of the molecular bridging entity must comprise a polynucleotide sequence. The polynucleotide sequence can be any chosen sequence provided that . . . if the recognizing portion . . . is itself a polynucleotide sequence, that it be sufficiently different from said recognizing sequence portion, to avoid hybrid formation between the analyte sequence and the second polynucleotide portion on the bridging entity . . .") Page 15, 2nd ¶ ("Specific examples of bridging entities . . . are covalently attached entities of . . . polynucleotides with polynucleotides.") Page 25, 2nd full ¶ ("The attachment of polynucleotide sequences to other polynucleotide sequences . . .") Page 25, last ¶ ("Other methods for attaching polynucleotides to polynucleotides . . .") Page 33, last ¶ (. . . open the DNA in the first container, incorporate any desired DNA probe present in the third container . . . ligate the polymer . . .")	Claims 20 and 115 ("wherein said polynucleotide sequence in said bridging entity is covalently attached to another polynucleotide sequence . . .") Claim 38 ("wherein said signalling entity is a polynucleotide polymer.")
326 (composition)	wherein said nucleic acid sequences or segments in the molecular bridging entity second portion are covalently attached to one another.	Page 9, last 3 lines ("Also present in the system is signalling entity 6 having thereon a polynucleotide portion 7 capable of annealing to polynucleotide portion 5 of the bridging entity 3.") Page 17, last ¶ ("The signalling entity of the invention needs to carry both a polynucleotide portion capable of annealing to the complementary portion on the bridging entity . . .") Page 15, 1st ¶ ("The polynucleotide portion on the signalling entity is defined by the same parameters as the complementary portion on the molecular bridging entity . . .") Page 15, 1st ¶ ("The polynucleotide portion on the signalling entity is defined by the same parameters as the complementary portion on the molecular bridging entity . . .") Page 15, 1st ¶ ("By 'polynucleotide' is meant to include both polynucleotides, polydeoxyribonucleotides, or any poly-purine, pyrimidine or analog and combinations thereof . . .")	Claim 18 ("wherein said polynucleotide sequence on said bridging entity comprises a poly deoxy G, poly deoxy C, poly deoxy T or poly deoxy A sequence, or any poly-ribo or -deoxyribo purine, pyrimidine or analog . . .")
327 (composition)	wherein said signalling entity nucleic acid portion comprises an oligo- or polynucleotide.	Page 15, 1st ¶ ("The polynucleotide portion on the signalling entity is defined by the same parameters as the complementary portion on the molecular bridging entity . . .") Page 15, 1st ¶ ("By 'polynucleotide' is meant to include both polynucleotides, polydeoxyribonucleotides, or any poly-purine, pyrimidine or analog and combinations thereof . . .")	Claim 18 ("wherein said polynucleotide sequence on said bridging entity comprises a poly deoxy G, poly deoxy C, poly deoxy T or poly deoxy A sequence, or any poly-ribo or -deoxyribo purine, pyrimidine or analog . . .")
328 (composition)	wherein said signalling entity oligo- or polynucleotide is selected from . . . an oligo- or polynucleotide, an oligo- or polydeoxyribonucleotide, a poly purine, a poly-pyrimidine and an analog-containing polymer . . .	Page 15, 1st ¶ ("The polynucleotide portion on the signalling entity is defined by the same parameters as the complementary portion on the molecular bridging entity . . .") Page 15, 1st ¶ ("By 'polynucleotide' is meant to include both polynucleotides, polydeoxyribonucleotides, or any poly-purine, pyrimidine or analog and combinations thereof . . .")	Claim 18 ("wherein said polynucleotide sequence on said bridging entity comprises a poly deoxy G, poly deoxy C, poly deoxy T or poly deoxy A sequence, or any poly-ribo or -deoxyribo purine, pyrimidine or analog . . .")

329 (composition)	wherein said oligo- or polynucleotide comprises a modified oligo- or polynucleotide.	Page 15,1st ¶ ("The polynucleotide portion on the signalling entity is defined by the same parameters as the complementary portion on the molecular bridging entity.") Page 20, last ¶, through Page 21, 1st ¶ ("A thorough description of various non-radioactive signal generating systems, both biotin/avidin-based and non-biotin/avidin-based can be found . . . fully incorporated by reference.") Page 21, 2nd ¶ (" . . . need not be a polynucleotide which has been chemically modified or artificially altered in any way . . .")	Claim 39 ("wherein said polynucleotide polymer is a naturally occurring modified DNA.") Claim 66 ("complexation between a signalling entity comprising a cloned insert on a naturally occurring modified DNA.")
330 (composition)	wherein said modified oligo- or polynucleotide comprises one or more nucleotides modified on the sugar, phosphate, base or combinations thereof.	Page 15,1st ¶ ("The polynucleotide portion on the signalling entity is defined by the same parameters as the complementary portion on the molecular bridging entity.") Page 20, last ¶, through Page 21, 1st ¶ ("A thorough description of various non-radioactive signal generating systems, both biotin/avidin-based and non-biotin/avidin-based can be found . . .") (See Claim 31,1 above)	Claim 30 ("wherein said DNA is single-stranded.") Claim 43 ("wherein said polymer is single-stranded.)
331 (composition)	wherein said signalling entity nucleic acid portion is single-stranded or partially double-stranded.	Page 15,1st ¶ ("The polynucleotide portion on the signalling entity is defined by the same parameters as the complementary portion on the molecular bridging entity.") Page 10, 2nd ¶ ("Bridging entity <u>11</u> , shown as a single-stranded circular polynucleotide polymer . . .") Page 11, 2nd ¶ ("nucleic acids or segments thereof, either single- or double-stranded.") Page 16, 2nd ¶ ("Among preferred bridging entities . . . are circular polymers of single- or double-stranded DNA . . .") Page 17, 1st full ¶ ("Ideally, a single-stranded DNA polymer can be provided . . .") Pages 57-61 (Example 32)	Claim 30 ("wherein said DNA is single-stranded.") Claim 43 ("wherein said polymer is single-stranded.)
332 (composition)	wherein said signalling entity nucleic acid portion is linear or circular.	Page 15,1st ¶ ("The polynucleotide portion on the signalling entity is defined by the same parameters as the complementary portion on the molecular bridging entity.") Page 10, 2nd ¶ ("Bridging entity <u>11</u> , shown as a single-stranded circular polynucleotide polymer.") Page 11, 2nd ¶ ("nucleic acids or segments thereof, either single- or double-stranded.") Page 16 ("Among preferred bridging entities . . . are circular polymers of single- or double-stranded DNA . . .")	Claims 29 and 124 ("wherein said bridging entity is a circular DNA polymer.")

333 (composition)	wherein said signalling entity nucleic acid portion is a polymer derived from a linear or circular nucleic acid molecule covalently attached to a signal generating portion or a signalling chemical moiety.	Page 19, last line, through Page 21, 1st ¶ ("The polynucleotide portion of the signalling entity can be covalently attached to biotin . . .") Page 22, last line, through Page 23, line 2 ("The signalling entity requires a polynucleotide portion and a signal generating portion.") Note: The term "signalling chemical moiety" is disclosed in Engelhardt et al., U.S. Pat. Appl. Ser. No. 391,440, filed June 23, 1982 and incorporated by reference at Page 21, 1st ¶. Pages 57-59, <u>Example 32 Use of Bacteriophage M13 as Bridging Entity</u> (See in particular Page 58, 2nd full ¶ ("The G(-) phage (signalling entity) is chemically reacted . . ." See also Page 59, No. 6 ("Polynucleotide kinase and ³² P-ATP are used to replace 5' ends with ³² P-phosphates.")) See also Claim 314 above taken with Page 15,1st ¶ ("The polynucleotide portion on the signalling entity is defined by the same parameters as the complementary portion on the molecular bridging entity."))	Claim 38 ("wherein said signalling entity is a polynucleotide polymer.") Claim 40 ("wherein said polynucleotide polymer is derived from a T (even) phage.") Claim 44 ("wherein said polymer is derived from a filamentous phage.") Claim 45 ("wherein said phage is M13 or a variant thereof.") Claim 133 ("wherein said signalling entity is a circular DNA polymer.") Claim 135 ("wherein said DNAs derived from a filamentous phage.") Claim 136 ("wherein said phage is M13 or a variant thereof.") Claim 149 ("wherein said signalling entity is derived from a filamentous phage.")
334 (composition)	wherein said signalling entity nucleic acid portion is derived from a phage selected from . . . a T even phage, a filamentous phage, and an M13 phage, or an M13 phage variant.	Page 15,1st ¶ ("The polynucleotide portion on the signalling entity is defined by the same parameters as the complementary portion on the molecular bridging entity.") Page 16, 2nd ¶ ("Among preferred bridging entities . . . are circular polymers . . . The single-stranded ones include so-called filamentous phages, such as fd, f1 and M13 . . .") Page 21, 2nd ¶ ("One such system is phage T4 . . . Other T (even) phages such as T2, T6, or T8 can also be used.") Pages 57-61, <u>Example 32 (Use of Bacteriophage M13 as Bridging Entity)</u>	Claim 40 ("wherein said T (even) phage is T4.") Claim 44 ("wherein said polymer is derived from a filamentous phage.") Claim 45 ("wherein said phage is M13 or a variant thereof.") Claim 133 ("wherein said signalling entity is a circular DNA polymer.") Claim 135 ("wherein said DNAs derived from a filamentous phage.") Claim 136 ("wherein said phage is M13 or a variant thereof.") Claim 149 ("wherein said signalling entity is derived from a filamentous phage.")
335 (composition)	wherein said signalling entity modified oligo- or polynucleotide comprises a naturally occurring modified oligo- or polynucleotide.	Page 21, 2nd ¶ ("In addition, the signal generating portion of the signalling entity need not be a polynucleotide which has been chemically modified or artificially altered in any way. Some biological systems perform <i>in vivo</i> modifications which can be utilized by this system . . .")	Claim 39 ("wherein said polynucleotide polymer is a naturally occurring modified DNA.") Claim 42 ("wherein said modified DNA carries a cloned insert.") Claim 66 ("wherein said step . . . comprises complexation between a signalling entity comprising a cloned insert on a naturally occurring modified DNA.")

336 (composition)	wherein said signalling entity modified oligo- or polynucleotide carries a cloned insert.	Page 21, 2nd ¶ ("It is possible to insert (clone) a low complexity repeating polynucleotide sequence into phage T4.") Pages 57-61, Example 32 (Use of Bacteriophage M13 as Bridging Entity)	Claim 42 ("wherein said modified DNA carries a cloned insert.") Claim 66 ("wherein said step . . . comprises complexation between a signalling entity comprising a cloned insert on a naturally occurring modified DNA.")
337 (composition)	wherein said signalling entity nucleic acid portion comprises a nucleic acid sequence or segment of repeating low complexity	Page 15, 1st ¶ ("The polynucleotide portion on the signalling entity is defined by the same parameters as the complementary portion on the molecular bridging entity") Page 15, 1st ¶ ("It is thus preferred to choose polynucleotide sequence portions . . . such as . . . any other low complexity (repeating) sequence.") Page 17, last 2 ¶s (" . . . the bridging entity comprises a DNA polymer which carries the sequence for a given gene . . . and, at another place in the polymer, a poly G, or poly GT, or poly dG, or poly dC, or poly dCA, or poly dGdT polynucleotide portion.") Page 27, 1st ¶ ("If the polynucleotide sequence comprises a strand of any one nucleotide (e.g., poly dG or poly dC) or a strand of any dinucleotide pair (e.g., poly dCdT, or the like.)")	Claims 36 ("wherein said polynucleotide portion on said signalling entity comprises . . . a repeating sequence of low complexity.") Claims 78 and 90 ("A DNA molecule carrying a polynucleotide portion which comprises . . . a repeating low-complexity polynucleotide.") Claim 131 ("wherein said polynucleotide portion on said signalling entity comprises . . . a low-complexity, repeating polynucleotide.")
338 (composition)	wherein said nucleic acid sequence or segment of repeating low complexity is selected from . . . a poly G or polydeoxy G, polyGT or polydeoxy GT, poly C or polydeoxy C, poly T or polydeoxy T, poly A or polydeoxy A, poly CA or polydeoxy CA, poly GA or polydeoxy GA, poly GAT or polydeoxy GAT, and poly GTA or polydeoxy GTA.	Page 15, 1st ¶ ("The polynucleotide portion on the signalling entity is defined by the same parameters as the complementary portion on the molecular bridging entity") Page 15, 1st ¶ ("It is thus preferred to choose polynucleotide sequence portions . . . such as, for example, poly deoxy G, poly deoxy A, poly deoxy GT, poly deoxy GA, poly deoxy GAT, poly deoxy GT, poly dCT, poly dAT, poly dG, poly dGA, poly dG, poly dC, poly dA, and a repeating sequence.") Page 17, last 2 ¶s (" . . . the bridging entity comprises a DNA polymer which carries the sequence for a given gene . . . and, at another place in the polymer, a poly G, or poly GT, or poly dG, or poly dC, or poly dCA, or poly dGdT polynucleotide portion.") Page 27, 1st ¶ ("If the polynucleotide sequence comprises a strand of any one nucleotide (e.g., poly dG or poly dC) or a strand of any dinucleotide pair (e.g., poly dCdT, or the like.)")	Claim 36 ("wherein said polynucleotide portion on said signalling entity comprises a poly deoxy C, poly deoxy G, poly deoxy A, poly deoxy T sequence, or a repeating sequence of low complexity.") Claim 90 ("The DNA molecule . . . which carries a polynucleotide portion which comprises a sequence selected from . . . poly dGT, poly dAC, poly dCT, poly dAT, poly dGC, poly dGA, poly dG, poly dC, poly dA, and a repeating low-complexity polynucleotide.") Claim 131 ("wherein said polynucleotide portion on said signalling entity comprises a poly dC, poly dG, poly dA, poly dT sequence, or a low-complexity, repeating polynucleotide.")

<p>339 (composition)</p> <p>wherein said signal generating portion or said one or more chemically modified or artificially altered polynucleotides are capable of directly providing a detectable signal.</p>	<p>Page 18, 2nd ¶ ("The 'signal generating portion' of the signalling entity . . . comprises a moiety which generates a signal itself (e.g., a radiolabel).") Page 20, 2nd ¶, through Page 21, 1st ¶ (referencing U.S. Pat. Appl. Serial Nos. 255,223 and 391,440)</p>	<p>Claim 46 ("wherein said signal generating portion of said signalling entity is radiolabeled.") Claim 50 ("wherein said signal generating portion comprises a fluorogenic compound") Claim 51 ("wherein said signal generating portion comprises an electron dense compound.") Note: The above dependent claims are examples of direct signalling or direct detection.</p>
<p>340 (composition)</p> <p>wherein said direct signal providing signal generating portion comprises a radioactive compound.</p>	<p>Page 18, 2nd ¶ ("It [signal generating portion] comprises a moiety which generates a signal itself (e.g., a radiolabel.)") Page 19, lines 1-2 ("Thus, the signal generating portion may comprise a radiolabel (e.g., ¹⁴C, ³²P, ³H and the like.)") Page 23, lines 4-8 ("covalent attachment of polynucleotides, or individual components thereof, to . . . 5) radiolabels.") Page 26, 2nd full ¶ ("The covalent incorporation of radiolabels . . .") Page 57, Example 31 <u>Synthesis of a Protein Coupled to a Signal Generating Polynucleotide. Example of IgG Coupled to Chemically Radio-labeled DNA</u> Pages 57-59, Example 32 <u>(Use of Bacteriophage M13 as Bridging Entity) (See Page 59, No. 6 "Polyribonucleotide kinase and ³²P-ATP are used to replace 5' ends with 32P-phosphates.)</u></p>	<p>Claim 46 ("wherein said signal generating portion of said signalling entity is radiolabeled.") Claim 94 ("The DNA molecule . . . wherein said signal generating moiety comprises a radiolabel") Claim 137 ("wherein said signal generating portion on said signalling entity is radiolabeled.")</p>

341 (composition)	<p>wherein said direct signal providing signal generating portion is selected from . . . a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound and an electron dense compound.</p> <p>Page 19, lines 1-4 ("Thus, the signal generating portion may comprise . . . a fluorescent label;")</p> <p>Page 19, 1st ¶ ("Thus, the signal generating portion may comprise . . . an electron dense compound such as ferritin (to be used with electron microscopy).")</p> <p>Page 32, last four lines, through Page 33, line 2 ("Other container means or series of container means may contain the elements necessary to generate the signal, such as . . . ferritin linked conjugates, . . . fluorogen linked conjugates and the like.")</p> <p>See also U.S. Pat. Appl. Ser. Nos. 255,223 filed on April 17, 1981 and 391,440, filed June 23, 1982, both cited on Pages 20-21. Each has culminated in the issuance of several U.S. patents, including U.S. Pat. Nos. 4,711,955 and 5,241,060. For example, U.S. Pat. No. 5,241,060 discloses a signalling moiety containing a fluorescing component (col. 24, lines 28-29); an electron dense component (col. 24, lines 34-36); a chemiluminescent component (col. 24, lines 47-50); an ion catalyzing a chromogenic reaction (col. 16, lines 8-9).</p>	<p>Claim 50 ("wherein said signal generating portion comprises a fluorogenic compound.")</p> <p>Claims 51 and 142 ("wherein said signal generating portion comprises an electron dense compound")</p> <p>Claim 58 ("wherein said step of detecting . . . comprises a fluorescence measurement, or electron microscopic measurement.")</p> <p>Claim 63 ("wherein said step of detecting . . . comprises detection of an electron dense compound")</p> <p>Claim 99 ("The DNA molecule . . . wherein said signal generating moiety(sic) comprises a fluorogenic compound.")</p> <p>Claim 141 ("wherein said signal generating portion comprises a fluorogen.")</p> <p>Claims 48 and 139 ("wherein said signal generating portion comprises an enzyme.")</p> <p>Claim 57 ("wherein said step of detecting . . . comprises an enzymatic reaction.")</p> <p>Claim 96 ("The DNA molecule . . . wherein said signal generating moiety comprises an enzyme.")</p>
342 (composition)	<p>wherein said direct signal providing signal generating portion comprises an enzyme.</p>	<p>Page 19, lines 1-4 ("Thus, the signal generating portion may comprise . . . an enzyme (e.g., peroxidase, alkaline or acid phosphatase, and the like).")</p>

<p>343 (composition)</p> <p>wherein said signal generating portion or said one or more chemically modified or artificially altered polynucleotides are indirectly capable of indirectly providing a detectable signal.</p>	<p>Page 18, 2nd ¶ ("[t]he signal generating portion] comprises . . . or a moiety which, upon further reaction or manipulation will give rise to a signal (e.g., an enzyme-linked system). Both types are herein called 'signal generating' portions.") Page 19, 2nd ¶ ("For example, if the signal generating portion . . . is an antigen, a signal can be generated by complexing . . . with an antibody/enzyme conjugate, followed by addition of enzyme substrate. If . . . an antibody, signal can be generated by complexing anti-antibody or an Fc binding protein . . .") Page 19, 3rd ¶ ("Among the preferred signal generating portions are those based on the biotin/avidin system. . .") Page 20, 1st ¶ ("Interaction of the biotin molecules in the signal generating portion with avidin, streptavidin or anti-avidin antibodies is then carried out . . . conjugated to such signalling components . . .") Page 20, 2nd ¶ through Page 21, 1st ¶ (citing U.S. Pat. Appl. Ser. Nos. 255,223 and 391,440; see Claim 341 above) Page 21, 2nd ¶ ("Detection could then be accomplished via a lectin/enzyme system, or lectin/fluorescent dye, or lectin/electron dense material.") Page 26, penultimate ¶ ("The preparation of the individual elements of the signal generating systems such as protein/latex conjugates, protein/ferritin conjugates, antibody/enzyme conjugates, fluorogen/antibody conjugates, avidin/enzyme conjugates, . . .")</p>	<p>Claims 48 and 139 ("wherein said signal generating portion comprises an enzyme.") Claim 54 ("wherein said signal generating portion comprises an antibody or antigen.") Claim 72 ("A polynucleotide sequence covalently attached to an antibody.") Claim 76 ("A polynucleotide sequence covalently attached to receptor.") Claim 96 ("wherein said signal generating moiety(sic) comprises an enzyme.") Claim 98 ("wherein said signal generating moiety(sic) comprises an antibody.") Claim 145 ("wherein said signal generating portion comprises an antibody.")</p>
<p>344 (composition)</p> <p>wherein said indirect signal providing signal generating portion is selected from . . . an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme.</p>	<p>Page 19, 1st ¶ ("Thus, the signal generating portion may comprise . . . an antibody (which may be used in a double antibody system), an antigen (to be used with a labeled antibody), a small molecule such as biotin (to be used with an avidin, streptavidin, or antibody system.)") Page 19, 2nd ¶; Page 19, 3rd ¶; Page 20, 1st ¶; Page 20, 2nd ¶ through Page 21, 1st ¶; Page 21, 2nd ¶; and Page 26, penultimate ¶ (See Claim 343 above)</p>	

345 (composition)	wherein said indirect signal providing signal generating portion comprises a polynucleotide sequence capable of recognizing a signal-containing moiety.	Page 69, Claim 59 ("wherein said signal generating portion is a polynucleotide sequence capable of recognizing a signal containing moiety.")	Claim 59 ("wherein said signal generating portion is a polynucleotide sequence capable of recognizing a signal containing moiety.")
346 (composition)	wherein said indirect signal providing signal generating portion comprises a compound capable of binding to an insoluble phase.	<p>Page 23, 1st ¶ ("the covalent attachment of polynucleotides, or individual components thereof, to . . . 6) insoluble phases such as bacterial phases, or latex particles.") Page 31, last 4 lines, through Page 32, 1st ¶ ("the 'signalling entity' is designed so that the signal generating portion comprises or is capable of specifically binding to an insoluble solid phase, such as a natural or synthetic aqueous insoluble resin, a glass, a plastic such as an acrylate or methacrylate, the inside of a test tube wall, or of a well, and the like. The bridging entity is allowed to incubate with the solid phase, thus creating recognition sites (i.e., affinity surfaces) for the analyte, which is then bound thereto.") Page 32, 2nd and 3rd line from the bottom of the page, through Page 33, 1st line ("the elements necessary to generate the signal . . . latex linked conjugates . . .")</p>	<p>Claims 52 and 143 ("wherein said signal generating portion comprises or binds to an insoluble phase.") Claims 53 and 144 ("wherein said insoluble phase comprises a latex particle, a resin, or a bacterium.") Claim 65 ("wherein said step of detecting a signal by means of said signal generating portion comprises a binding step on an insoluble phase.")</p>
347 (composition)	wherein said signal generating portion or said one or more chemically modified or artificially altered polynucleotides are capable of being detected by a member selected from . . . an enzymatic measurement, a fluorescent measurement, a phosphorescent measurement, a chemiluminescent measurement, a colorimetric measurement, a microscopic measurement, an electron density measurement, a radioactive measurement and a binding step on an insoluble phase.	<p>Page 29, 1st ¶ ("complex . . . is allowed to incubate with the enzyme carrying reagent . . . and substrate is added thereto to develop color. Alternatively, enzyme might be attached directly to the polynucleotide strand on the signalling entity, . . . substrate is added immediately to obtain color development.") Also Fig. 2 ("Color Detection")</p> <p>Claim 56 ("wherein said step of detecting a signal . . . comprises a radioactivity measurement.") Claim 57 ("wherein said step of detecting a signal . . . comprises an enzymatic measurement.") Claim 58 ("wherein said step of detecting a signal . . . comprises a fluorescence measurement, or electron microscopic measurement.") Claim 63 ("wherein said step of detecting a signal . . . comprises detection of an electron dense compound.") Claim 65 ("wherein said step of detecting a signal by means of said signal generating portion comprises a binding step on an insoluble phase.")</p>	<p>Claim 56 ("wherein said step of detecting a signal by means of said signal generating portion comprises a radioactivity measurement.") Claim 57 ("wherein said step of detecting a signal by means of said signal generating portion comprises an enzymatic measurement.") Claim 58 ("wherein said step of detecting a signal by means of said signal generating portion comprises a fluorescence measurement, or electron microscopic measurement.") Claim 63 ("wherein said step of detecting a signal by means of said signal generating portion comprises a binding step on an insoluble phase.")</p>

348 (composition)	wherein the ratio of the nucleic acid sequences or segments in the second portion to the first portion of the molecular bridging entity is greater than 5.	Page 16, 1st ¶ ("There may be many more polynucleotide sequences portions than recognizing portions, or vice versa. In the case when the ratio of polynucleotide sequence portion to recognizing portion on the bridging entity is greater than 1, for example, 5, 10 or greater . . .") <i>ibid</i> ("10 or greater . . .")
349 (composition)	wherein the ratio is greater than 10	Page 22, 1st ¶ ("When the ratio of signal generating portions to polynucleotide portion in the signalling portion of the signalling entity is greater than 1 (e.g. greater than 5, or greater than 10).")
350 (composition)	wherein the ratio of the signal generating portions or the one or more chemically modified or artificially altered polynucleotides to the nucleic acid portion in any or all of the signalling entities is greater than 1	Page 22, 1st ¶ ("When the ratio of signal generating portions to polynucleotide portion in the signalling portion of the signalling entity is greater than 1 (e.g. greater than 5, or greater than 10).")
351 (composition)	wherein the ratio is greater than 5.	<i>ibid</i> ("greater than 5")
352 (composition)	wherein the ratio is greater than 10.	<i>ibid</i> ("greater than 10")
353 (composition)	wherein both the ratio of the nucleic acid sequences or segments in the second portion to the first portion of the molecular bridging entity is greater than 1, and the ratio of the signal generating portions or the one or more chemically modified or artificially altered polynucleotides to the nucleic acid portion in any or all of the signalling entities are greater than 1.	Page 22, 1st ¶ ("When the ratio of signal generating portions to polynucleotide portion in the signalling portion of the signalling entity is greater than 1 . . . the system functions as an amplification system . . . If, in addition, the bridging entity has a signal amplification system itself, i.e., the ratio of polynucleotide portions to recognizing portions on the bridging entity is greater than 1, the overall signal amplification system is the product of both ratios.")
354 (composition)	wherein one or both ratios are greater than 5	Page 16, 1st ¶ (See Claim 348 above) Page 22, 1st ¶ (See Claims 350, 351 and 353 above)
355 (composition)	wherein one or both ratios are greater than 10	Page 22, 1st ¶ (See Claims 350, 352 and 353 above)

356 (composition)	wherein the ratio of signalling entities to molecular bridging entity is greater than 5.	Page 4 ("The prior art has also utilized amplification techniques, wherein the signalling event is related to the primary recognition event in a ratio greater than 1:1. Thus, the signalling component of the assay may be present in a ratio of 10:1 to each recognition component, thereby providing a 10-fold increase in sensitivity.") Page 6 ("It would therefore be very useful to develop an assay system which . . . would utilize the great versatility of polynucleotide-based sequence recognition, and include the possibility of signal amplification methods.") See also Page 16, 1st ¶ and Page 22, 1st ¶, discussed <i>supra</i> . <i>Ibid.</i>
357 (composition)	wherein the ratio is greater than 10.	Page 28, 1st ¶ ("The analyte, together with impurifying materials, if such be the case, can be tested in the mixture as purified or, especially when it is a nucleic acid segment, can be immobilized (see for example, Wahl et al U.S. Patent 4,302,204.)")
358 (composition)	wherein the analyte is immobilized	<i>Ibid.</i> Also Page 8, penultimate paragraph ("The invention provides, in addition to the aforementioned process, various elements and components to be used therein, such as various molecular bridging entities. . . . as well as kits comprising such entities, and other components for use in the process.") Also Page 9, 1st full ¶ ("Uses for the process, system and components are unlimited, and include all of the uses to which prior art assay techniques have been put, as well as generally, the detection of any analyte capable of recognition, in any sample.") Page 32, 1st ¶ ("The bridging entity is allowed to incubate with the solid phase, thus creating recognition sites (i.e., affinity surfaces) for the analyte, which is then bound thereto.")

360 (article of manufacture)	An article of manufacture . . . a molecular bridging entity comprising a first portion . . . and a second portion comprising one or more nucleic acid sequences or segments; and more than one signalling entity each such entity comprising a nucleic acid portion . . . and one or more signal generating portions, each capable of providing a detectable signal.	"An article of manufacture" is a statutorily recognized class of patentable subject matter. See 35 U.S.C. §101. See Claim 283 above. See Claim 283 above
361 (article of manufacture)	An article of manufacture . . . a molecular bridging entity comprising a first portion . . . and a second portion comprising one or more nucleic acid sequences; and more than one signalling entity each such entity comprising a nucleic acid portion . . . and one or more polynucleotides which have been chemically modified or artificially altered	"An article of manufacture" is a statutorily recognized class of patentable subject matter. See 35 U.S.C. §101. See Claim 291 above. See Claim 291 above.
362 (article of manufacture)	further comprising the analyte	Page 7 (2nd full ¶) ("the analyte is present in the sample) Page 10, lines 3-10 (lines 3-6 in particular) ("When analyte is present in the sample being analyzed . . .") Page 11, 1st full ¶ ("The term 'analyte' . . . includes any substances or substances either alone or in admixtures . . .")

363 (detection process)	<p>A process for detecting an analyte having one or more molecularly recognizable portions thereon,</p> <p>providing the composition</p> <p>forming a complex comprising said composition and said analyte; and</p> <p>detecting said analyte by a signal provided by said signal generating portion or portions present in said complex.</p> <p>characterized in that said forming step comprises contacting said analyte with said bridging entity to form a first complex and thereafter contacting the first complex with said signalling entity to form said complex.</p>	<p>Page 7, 2nd ¶ through Page 8, line 13 ("The process of the invention comprises a method of detecting in a sample an analyte (A) having a molecularly recognizable portion thereon, which comprises")</p> <p>Page 7, line 13 to end of page ("providing a molecular bridging entity (B)")</p> <p>Page 8, lines 4-11 ("forming a complex comprising")</p> <p>Page 8, lines 12-13 ("detecting a signal by means of said signal generating portion present in said complex")</p>	<p>Claim 1 ("A method of detecting in a sample an analyte (A) having a molecularly recognizable portion thereon, which comprises providing forming a complex and detecting a signal")</p> <p><i>ibid.</i></p>
364 (process)	<p>characterized in that said forming step comprises contacting said analyte with said bridging entity to form a first complex and thereafter contacting the first complex with said signalling entity to form said complex.</p>	<p>Page 10, 1st ¶ ("When analyte is present in the sample being analyzed, interaction occurs with bridging entity 3 through the recognizable and recognition portions 2 and 4, respectively. The complex formed thereby is then annealed through the polynucleotide portion 5, to the complementary polynucleotide portion 7 on the signalling entity, which brings the signalling portion 8 into some stoichiometric relation with the analyte 1.")</p> <p>Page 10, 2nd ¶ ("Presence of the DNA sequence 10 in the sample being analyzed causes the bridging entity 11 to hybridize thereto, and subsequent annealing of the signalling entity to the thus formed complex attaches the biotin portion, through the network, to the analyte.")</p> <p>Page 28, 2nd ¶ ("The composition suspected of containing the analyte is incubated with the bridging entity for a time and under conditions sufficient to allow complexation between the recognizable portion of the analyte and the recognizing portion on the bridging entity.")</p>	<p>Page 10, 1st ¶ ("When analyte is present in the sample being analyzed, interaction occurs with bridging entity 3 through the recognizable and recognition portions 2 and 4, respectively. The complex formed thereby is then annealed through the polynucleotide portion 5, to the complementary polynucleotide portion 7 on the signalling entity, which brings the signalling portion 8 into some stoichiometric relation with the analyte 1.")</p> <p>Page 10, 2nd ¶ ("Presence of the DNA sequence 10 in the sample being analyzed causes the bridging entity 11 to hybridize thereto, and subsequent annealing of the signalling entity to the thus formed complex attaches the biotin portion, through the network, to the analyte.")</p> <p>Page 28, 2nd ¶ ("The composition suspected of containing the analyte is incubated with the bridging entity for a time and under conditions sufficient to allow complexation between the recognizable portion of the analyte and the recognizing portion on the bridging entity.")</p> <p><i>ibid.</i></p>
365 (process)	<p>characterized in that said forming step comprises contacting said bridging entity with said signalling entity to form a first complex and thereafter contacting the first complex with said analyte to form said complex.</p>	<p>Page 33, last ¶ through Page 34, 1st ¶ ("Thus, the user would utilize a cleavage method . . . to open the DNA in the first container, incorporate any desired DNA probe present in the third container or container series, ligate the polymer and then utilize the bridging entity and the signalling entity to detect and identify the presence of any desired genetic sequence present in the analyte")</p>	<p>Page 33, last ¶ through Page 34, 1st ¶ ("Thus, the user would utilize a cleavage method . . . to open the DNA in the first container, incorporate any desired DNA probe present in the third container or container series, ligate the polymer and then utilize the bridging entity and the signalling entity to detect and identify the presence of any desired genetic sequence present in the analyte")</p> <p><i>ibid.</i></p>

<p>366 (process)</p> <p>wherein detecting is directly carried out by means of a detectable signal provided by said signal generating portion.</p>	<p>Page 18, 2nd ¶ ("The signal generating portion of the signalling entity . . . comprises a moiety which generates a signal itself (e.g., a radiolabel),") Page 20, 2nd ¶, through Page 21, 1st ¶ (referencing U.S. Pat. Appl. Serial Nos. 255,223 and 391,440)</p>	<p>Claim 46 ("wherein said signal generating portion of said signalling entity is radiolabelled.") Claim 50 ("wherein said signal generating portion comprises a fluorogenic compound.") Claim 51 ("wherein said signal generating portion comprises an electron dense compound.") Note: The above dependent claims are examples of direct signalling or direct detection.</p>
<p>367 (process)</p> <p>wherein said detecting step the direct detectable signal provided by said signal generating portion comprises a radioactive compound.</p>	<p>Page 18, 2nd ¶ ("[signal generating portion] comprises a moiety which generates a signal itself (e.g., a radiolabel).") Page 19, lines 1-2 ("Thus, the signal generating portion may comprise a radiolabel (e.g., ¹⁴C, ³²P, ³H and the like).") Page 23, lines 4-8 ("covalent attachment of polynucleotides, or individual components thereof, to . . . 5) radiolabels.") Page 26, 2nd full ¶ ("The covalent incorporation of radiolabels . . .") Page 57, <u>Example 31</u> (<u>Synthesis of a Protein Coupled to a Signal Generating Polynucleotide. Example of IgG Coupled to Chemically Radio-labeled DNA</u>) Pages 57-59 <u>Example 32</u> (<u>Use of Bacteriophage M13 as Bridging Entity</u>) (See Page 59, No. 6. "Polynucleotide kinase and ³²P-ATP are used to replace 5' ends with 32P-phosphates.")</p>	<p>Claim 46 ("wherein said signal generating portion of said signalling entity is radiolabelled.") Claim 94 ("The DNA molecule . . . wherein said signal generating moiety comprises a radiolabel") Claim 137 ("wherein said signal generating portion on said signalling entity is radiolabelled.")</p>

368 (process)	<p>wherein said detecting step the direct detectable signal is provided by a member selected from . . . a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound and an electron dense compound.</p>	<p>Page 19, lines 1-4 ("Thus, the signal generating portion may comprise . . . a fluorescent label.") Page 19, 1st ¶ ("Thus, the signal generating portion may comprise . . . an electron dense compound such as ferritin (to be used with electron microscopy).") Page 32, last four lines, through Page 33, line 2 ("Other container means or series of container means may contain the elements necessary to generate the signal, such as . . . ferritin linked conjugates, . . . fluorogen linked conjugates and the like.") See also U.S. Pat. Appl. Ser. Nos. 255,223, filed on April 17, 1981 and 391,440 filed June 23, 1982, both cited on Pages 20-21. Each has culminated in the issuance of several U.S. patents, including U.S. Pat. Nos. 4,711,955 and 5,241,060. For example, U.S. Pat. No. 5,241,060 discloses a signalling moiety containing a fluorescing component (col. 24, lines 28-29); an electron dense component (col. 24, lines 34-36); a chemiluminescent component (col. 24, lir. 47-50); an ion catalyzing a chromogenic reaction (col. 16, lines 8-9).</p>	<p>Claim 50 ("wherein said signal generating portion comprises a fluorogenic compound.") Claims 51 and 142 ("wherein said signal generating portion comprises an electron dense compound.") Claim 58 ("wherein said step of detecting . . . comprises a fluorescence measurement, or electron microscopic measurement.") Claim 63 ("wherein said step of detecting . . . comprises detection of an electron dense compound.") Claim 99 ("The DNA molecule . . . wherein said signal generating moiety(sic) comprises a fluorogenic compound.") Claim 141 ("wherein said signal generating portion comprises a fluorogen.")</p>
369 (process)	<p>wherein said detecting step the signal generating portion comprises an enzyme.</p>	<p>Page 19, lines 1-4 ("Thus, the signal generating portion may comprise . . . an enzyme (e.g., peroxidase, alkaline or acid phosphatase, and the like).")</p>	<p>Claims 48 and 139 ("wherein said signal generating portion comprises an enzyme.") Claim 57 ("wherein said step of detecting . . . comprises an enzymatic reaction.") Claim 96 ("The DNA molecule . . . wherein said signal generating moiety comprises an enzyme.")</p>

<p>370 (process)</p> <p>wherein detecting is indirectly carried out by means of a detectable signal provided by said signal generating portion.</p>	<p>Page 18, 2nd ¶ ("It [the signal generating portion] comprises . . . or a moiety which, upon further reaction or manipulation will give rise to a signal (e.g., an enzyme-linked system). Both types are herein called 'signal generating' portions.")</p> <p>Page 19, 2nd ¶ ("For example, if the signal generating portion . . . is an antigen, a signal can be generated by complexing . . . with an antibody/enzyme conjugate, followed by addition of enzyme substrate. If . . . an antibody, signal can be generated by complexing anti-antibody or an Fc binding protein . . .")</p> <p>Page 19, 3rd ¶ ("Among the preferred signal generating portions are those based on the biotin/avidin system. . .")</p> <p>Page 20, 1st ¶ ("Interaction of the biotin molecules in the signal generating portion with avidin, streptavidin or anti-biotin antibodies is then carried out . . . conjugated to such signalling components . . .")</p> <p>Page 20, 2nd ¶ through Page 21, 1st ¶ (citing U.S. Pat. Appl. Ser. Nos. 255,223 and 391,440; see Claim 341 above)</p> <p>Page 21, 2nd ¶ ("Detection could then be accomplished via a lectin/enzyme system, or lectin/fluorescent dye, or lectin/electron dense material.")</p> <p>Page 26, penultimate ¶ ("The preparation of the individual elements of the signal generating systems such as protein/latex conjugates, protein/ferritin conjugates, antibody/enzyme conjugates, fluorogen/antibody conjugates, avidin/enzyme conjugates, . . .")</p>	<p>Claims 48 and 139 ("wherein said signal generating portion comprises an enzyme.")</p> <p>Claim 54 ("wherein said signal generating portion comprises an antibody or antigen.")</p> <p>Claim 72 ("A polynucleotide sequence covalently attached to an antibody.")</p> <p>Claim 76 ("A polynucleotide sequence covalently attached to receptor . . .")</p> <p>Claim 96 ("wherein said signal generating moiety(sic) comprises an enzyme.")</p> <p>Claim 98 ("wherein said signal generating moiety(sic) comprises an antibody.")</p> <p>Claim 145 ("wherein said signal generating portion comprises an antibody . . .")</p>
<p>371 (process)</p> <p>wherein said detecting step the signal generating portion is selected from . . . an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme.</p>	<p>Page 19, 1st ¶ ("Thus, the signal generating portion may comprise . . . an antibody (which may be used in a double antibody system), an antigen (to be used with a labeled antibody), a small molecule such as biotin (to be used with an avidin, streptavidin, or antibiotin system).")</p> <p>Page 19, 2nd ¶; Page 19, 3rd ¶; Page 20, 1st ¶; Page 20, 2nd ¶; through Page 21, 1st ¶; Page 21, 2nd ¶; and Page 26, penultimate ¶ (See Claim 343 above)</p>	

372 (process)	wherein said detecting step the signal generating portion comprises a polynucleotide sequence capable of recognizing a signal-containing moiety.	Page 69, Claim 59 ("wherein said signal generating portion is a polynucleotide sequence capable of recognizing a signal containing moiety.")	Claim 59 ("wherein said signal generating portion is a polynucleotide sequence capable of recognizing a signal containing moiety.")
373 (process)	wherein said detecting step the signal generating portion comprises a compound capable of binding to an insoluble phase.	<p>Page 23, 1st ¶ ("the covalent attachment of polynucleotides, or individual components thereof, to . . . 6) insoluble phases such as bacterial phases, or latex particles.")</p> <p>Page 31, last 4 lines, through Page 32, 1st ¶ ("the 'signalling entity' is designed so that the signal generating portion comprises or is capable of specifically binding to an insoluble solid phase, such as a natural or synthetic aqueous insoluble resin, a glass, a plastic such as an acrylate or methacrylate, the inside of a test tube wall, or of a well, and the like. The bridging entity is allowed to incubate with the solid phase, thus creating recognition sites (i.e., affinity surfaces) for the analyte, which is then bound thereto.")</p> <p>Page 32, 2nd and 3rd line from the bottom of the page, through Page 33, 1st line ("the elements necessary to generate the signal . . . latex linked conjugates . . .")</p>	<p>Claims 52 and 143 ("wherein said signal generating portion comprises or binds to an insoluble phase")</p> <p>Claims 53 and 144 ("wherein said insoluble phase comprises a latex particle, a resin, or a bacterium.")</p> <p>Claim 65 ("wherein said step of detecting a signal by means of said signal generating portion comprises a binding step on an insoluble phase")</p>
374 (process)	wherein said signal generating portion is capable of being detected by a member selected from . . . an enzymatic measurement, a fluorescent measurement, a phosphorescent measurement, a chemiluminescent measurement, a colorimetric measurement, a microscopic measurement, an electron density measurement, a radioactive measurement and a binding step on an insoluble phase.	<p>Page 29, 1st ¶ ("complex . . . is allowed to incubate with the enzyme carrying reagent . . . and substrate is added thereto to develop color. Alternatively, enzyme might be attached directly to the polynucleotide strand on the signalling entity . . . substrate is added immediately to obtain color development.")</p> <p>Also Fig. 2 ("Color Detection")</p> <p>Claim 56 ("wherein said step of detecting a signal . . . comprises a radioactivity measurement")</p> <p>Claim 57 ("wherein said step of detecting a signal . . . comprises an enzymatic measurement")</p> <p>Claim 58 ("wherein said step of detecting a signal . . . comprises a fluorescence measurement, or electron microscopic measurement")</p> <p>Claim 63 ("wherein said step of detecting a signal . . . comprises detection of an electron dense compound")</p> <p>Claim 65 ("wherein said step of detecting a signal by means of said signal generating portion comprises a binding step on an insoluble phase")</p>	<p>Claim 56 ("wherein said step of detecting a signal by means of said signal generating portion comprises a radioactivity measurement")</p> <p>Claim 57 ("wherein said step of detecting a signal by means of said signal generating portion comprises an enzymatic measurement")</p> <p>Claim 58 ("wherein said step of detecting a signal by means of said signal generating portion comprises a fluorescence measurement, or electron microscopic measurement")</p> <p>Claim 63 ("wherein said step of detecting a signal by means of said signal generating portion comprises a binding step on an insoluble phase")</p>

375 (process)	wherein the analyte is fixed or immobilized.	Page 28, 1st ¶ ("The analyte, together with impurifying materials if such be the case, can be tested in the mixture as purified or, especially when it is a nucleic acid segment, can be immobilized (see for example, Wahl et al U.S. Patent 4,302,204.)")
376 (process)	wherein fixing or immobilizing the analyte takes place before forming the complex.	Page 28, 1st and 2nd ¶s ("The analyte, together with impurifying materials if such be the case, can be tested in the mixture as purified or, especially when it is a nucleic acid segment, can be immobilized (see for example, Wahl et al U.S. Patent 4,302,204.) The composition suspected of containing the analyte is incubated with the bridging entity for a time and under conditions sufficient to allow complexation between the recognizable portion of the analyte and the recognizing portion on the bridging entity.")
377 (process)	wherein fixing or immobilizing the analyte takes place after forming the complex.	Page 28, 2nd ¶ ("Normally, after complexation has occurred, the sample is washed with neutral solution to remove excess bridging entity.") Note: Washing is only carried out if immobilization has occurred, in this case, after immobilization of the analyte following complexation.
378 (process)	further comprising one or more washing steps	Page 28, 2nd ¶ ("Normally, after complexation has occurred, the sample is washed with neutral solution to remove excess bridging entity... Alternatively, ... a wash is carried out after annealing has occurred between the polynucleotide strands on the bridging entity and on the signalling entity respectively... A final wash may be necessary prior to generation of signal.")

379 (process)	wherein the molecular bridging entity is immobilized.	<p>Page 28, 1st ¶ ("The analyte, together with impurifying materials if such be the case, can be tested in the mixture as purified or, especially when it is a nucleic acid segment, can be immobilized (see for example, Vahli et al U.S. Patent 4,302,204.)")</p> <p>Also Page 8, penultimate paragraph ("The invention provides, in addition to the aforementioned process, various elements and components to be used therein, such as various molecular bridging entities . . . as well as kits comprising such entities, and other components for use in the process . . .")</p> <p>Also Page 9, 1st full ¶ ("Uses for the process, system and components are unlimited, and include all of the uses to which prior art assay techniques have been put, as well as generally, the detection of any analyte capable of recognition, in any sample . . .")</p> <p>Page 32, 1st ¶ ("The bridging entity is allowed to incubate with the solid phase, thus creating recognition sites (i.e., affinity surfaces) for the analyte, which is then bound thereto . . .")</p> <p>Page 28, 2nd ¶ ("Normally, after complexation has occurred, the sample is washed with neutral solution to remove excess bridging entity . . . Alternatively, . . . a wash is carried out after annealing has occurred between the polynucleotide strands on the bridging entity and on the signalling entity respectively . . . A final wash may be necessary prior to generation of signal . . .")</p>	<p>Same as Claim 363 above.</p>
380 (process)	further comprising one or more washing steps		
381 (detection process)	<p>providing the composition . . .</p> <p>forming a complex comprising the components of said composition and said analyte;</p> <p>detecting said analyte by a signal provided by said signal generating portion or portions present in said complex.</p>		<p>Same as Claim 363 above.</p>

382 (process)	characterized in that said forming step comprises contacting said analyte with said bridging entity to form a first complex and thereafter contacting the first complex with said signalling entity to form said complex.	Same as Claim 364 above.	Same as Claim 364 above.
383 (process)	characterized in that said forming step comprises contacting said bridging entity with said signalling entity to form a first complex and thereafter contacting the first complex with said analyte to form said complex.	Same as Claim 365 above.	Same as Claim 365 above.
384 (process)	wherein detecting is directly carried out by means of a detectable signal provided by said signal generating portion.	Same as Claim 366 above.	Same as Claim 366 above.
385 (process)	wherein said detecting step the direct detectable signal provided by said signal generating portion comprises a radioactive compound.	Same as Claim 367 above.	Same as Claim 367 above.
386 (process)	wherein said detecting step the direct detectable signal is provided by a member selected from . . . a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound and an electron dense compound.	Same as Claim 368 above.	Same as Claim 368 above.
387 (process)	wherein said detecting step the signal generating portion comprises an enzyme.	Same as Claim 369 above.	Same as Claim 369 above.
388 (process)	wherein detecting is indirectly carried out by means of a detectable signal provided by said signal generating portion.	Same as Claim 370 above.	Same as Claim 370 above.

389 (process)	wherein said detecting step the signal generating portion is selected from . . . an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme.	Same as Claim 371 above.	Same as Claim 371 above.
390 (process)	wherein said detecting step the signal generating portion comprises a polynucleotide sequence capable of recognizing a signal-containing moiety.	Same as Claim 372 above.	Same as Claim 372 above.
391 (process)	wherein said detecting step the signal generating portion comprises a compound capable of binding to an insoluble phase.	Same as Claim 373 above	Same as Claim 373 above
392 (process)	wherein said signal generating portion is capable of being detected by a member selected from . . . an enzymatic measurement, a fluorescent measurement, a phosphorescent measurement, a chemiluminescent measurement, a colorimetric measurement, a microscopic measurement, an electron density measurement, a radioactive measurement and a binding step on an insoluble phase.	Same as Claim 374 above.	Same as Claim 374 above.
393 (process)	wherein the analyte is fixed or immobilized.	Same as Claim 375 above.	Same as Claim 375 above
394 (process)	wherein fixing or immobilizing the analyte takes place before forming the complex.	Same as Claim 376 above.	Same as Claim 376 above
395 (process)	wherein fixing or immobilizing the analyte takes place after forming the complex.	Same as Claim 377 above.	Same as Claim 377 above.
396 (process)	further comprising one or more washing steps.	Same as Claim 378 above.	Same as Claim 378 above.
397 (process)	wherein the molecular bridging entity is immobilized	Same as Claim 379 above.	Same as Claim 379 above

398 (process)	further comprising one or more washing steps providing the composition . . .	Same as Claim 380 above.	Same as Claim 380 above.
399 (detection process)	fixing or immobilizing said analyte or a sample containing said analyte to a solid support.	See Claim 363 above. Page 28, 1st ¶ ("The analyte, together with impurifying materials if such be the case, can be tested in the mixture as purified or, especially when it is a nucleic acid segment, can be immobilized (see for example, <u>Wahl et al U.S. Patent 4,302,204.</u> ")	See Claim 363 above.
400 (process)	forming a complex comprising said composition and said analyte, and detecting said analyte by a signal provided by said signal generating portion or portions present in said complex.	See Claim 363 above.	Claim 1 ("A method of detecting in a sample an analyte (A) having a molecularly recognizable portion thereon, which comprises: . . . providing . . . forming a complex . . . and detecting a signal"),
401 (process)	characterized in that said forming step comprises contacting said fixed or immobilized analyte with said bridging entity to form a first complex and thereafter contacting the first complex with said signalling entity to form said complex comprising said composition and said analyte	Same as Claim 364 above.	Claim 1 ("A method of detecting in a sample an analyte (A) having a molecularly recognizable portion thereon, which comprises: . . . providing . . . forming a complex . . . and detecting a signal").
	characterized in that said forming step comprises contacting said bridging entity with said signalling entity to form a first complex and thereafter contacting the first complex with said fixed or immobilized analyte to form said complex comprising said composition and said analyte.	Same as Claim 365 above.	Claim 1 ("A method of detecting in a sample an analyte (A) having a molecularly recognizable portion thereon, which comprises: . . . providing . . . forming a complex . . . and detecting a signal").

402 (process)	further comprising one or more washing steps prior to detection.	Page 28, 2nd ¶ ("Normally, after complexation has occurred, the sample is washed with neutral solution to remove excess bridging entity . . . Alternatively, . . . a wash is carried out after annealing has occurred between the polynucleotide strands on the bridging entity and on the signalling entity respectively . . . A final wash may be necessary prior to generation of signal.") <i>ibid.</i>	
403 (process)	further comprising one or more washing steps prior to detection.	<i>ibid.</i>	
404 (process)	further comprising one or more washing steps prior to detection.	<i>ibid.</i>	
405 (detection process)	fixing or immobilizing said analyte or a sample containing said analyte to a solid support.	Page 28, 1st ¶ ("The analyte, together with impurifying materials if such be the case, can be tested in the mixture as purified or, especially when it is a nucleic acid segment, can be immobilized (see for example, Wahl et al U.S. Patent 4,302,204.)") providing the composition . . . forming a complex comprising said composition and said analyte.	See Claim 363 above. See Claim 363 above.
406 (process)	detecting said analyte by means of the one or more chemically modified or artificially altered polynucleotides present in said complex.	characterized in that said forming step comprises contacting said fixed or immobilized analyte with said bridging entity to form a first complex and thereafter contacting the first complex with said signalling entity to form said complex comprising said composition and said analyte.	Same as Claim 364 above. Same as Claim 364 above.

			Same as Claim 365 above	
407 (process)	characterized in that said forming step comprises contacting said bridging entity with said signalling entity to form a first complex and thereafter contacting the fixed or immobilized analyte with the first complex to form said complex comprising said composition and said analyte.			Same as Claim 365 above
408 (process)	further comprising one or more washing steps prior to detection.	Same as Claim 378 above.		Same as Claim 378 above.
409 (process)	further comprising one or more washing steps prior to detection	<i>ibid.</i>	<i>ibid.</i>	<i>ibid.</i>
410 (process)	further comprising one or more washing steps prior to detection.	<i>ibid.</i>	<i>ibid.</i>	<i>ibid.</i>
411 (kit)	A kit . . . comprising as components thereof:	Page 8, penultimate ¶ ("The invention provides . . . various molecular elements and components to be used therein, such as various molecular bridging entities, and various signalling entities, as well as kits comprising said entities.") Also Page 32, 2nd ¶, through Page 33 ("The present invention lends itself readily to the preparation of kits comprising one or more of the elements necessary to perform the detection and identification process . . .")	Claim 100 ("A kit useful for the detection of an analyte (A) having a molecularly recognizable portion thereon, comprising . . .")	See composition Claim 283 above.
				See composition Claim 283 above.
				See composition Claim 283 above.

412 (kit)	<p>A kit . . . comprising as components thereof:</p> <p>a container carrying a complex which comprises:</p> <p>a molecular bridging entity comprising a first portion . . . and a second portion comprising one or more nucleic acid sequences; and</p> <p>more than one signalling entity, each such entity comprising a nucleic acid portion . . . and one or more signal generating portions, each such portion being capable of providing a detectable signal.</p>	<p>Page 8, penultimate ¶ (See Claim 411 above) Page 32, 2nd ¶, through Page 33 (See Claim 411 above)</p> <p>See composition Claim 285 above.</p>	<i>ibid.</i>
413 (kit)	<p>A kit . . . comprising as components thereof:</p> <p>a container carrying more than one molecular bridging entity, each such entity comprising a first portion . . . and a second portion comprising one or more nucleic acid sequences or segments; and</p> <p>a container carrying more than one signalling entity, each such entity comprising a nucleic acid portion . . . and one or more signal generating portions capable of providing a detectable signal.</p>	<p>Page 8, penultimate ¶ (See Claim 411 above) Page 32, 2nd ¶, through Page 33 (See Claim 411 above)</p> <p>See composition Claim 287 above.</p> <p>See composition Claim 287 above.</p>	<i>ibid.</i>

414 (kit)	A kit . . . comprising as components thereof: more than one molecular bridging entity, each such entity comprising a first portion . . . and a second portion comprising one or more nucleic acid sequences or segments; and more than one signalling entity, each such entity comprising a nucleic acid portion . . . and one or more signal generating portions capable of providing a detectable signal.	Page 8, penultimate ¶ (See Claim 411 above) Page 32, 2nd ¶ through Page 33 (See Claim 411 above) See composition Claim 287 above.
415 (kit)	A kit . . . comprising as components thereof: a complex which comprises: (i) more than one molecular bridging entity, each such entity comprising a first portion . . . and a second portion comprising one or more nucleic acid sequences or segments; and (ii) more than one signalling entity, each such entity comprising a nucleic acid portion . . . and one or more signal generating portions capable of providing a detectable signal	Page 8, penultimate ¶ (See Claim 411 above), Page 32, 2nd ¶, through Page 33 (See Claim 411 above) See composition Claim 289 above. See composition Claim 289 above. <i>ibid.</i>

416 (kit)	A kit . . . comprising as components thereof a molecular bridging entity . . . and a second portion comprising one or more nucleic acid sequences or segments, and more than one signalling entity, each such entity comprising a nucleic acid portion . . . and one or more polynucleotides which have been chemically modified or artificially altered	Page 8, penultimate ¶ (See Claim 411 above) Page 32, 2nd ¶, through Page 33 (See Claim 411 above) See composition Claim 291 above.	<i>ibid</i>
417 (kit)	A kit . . . comprising as components thereof a complex which comprises: a molecular bridging entity . . . and a second portion comprising one or more nucleic acid sequences or segments, and more than one signalling entity, each such entity comprising a nucleic acid portion . . . and one or more polynucleotides which have been chemically modified or artificially altered	Page 8, penultimate ¶ (See Claim 411 above) Page 32, 2nd ¶, through Page 33 (See Claim 411 above) See composition Claim 292 above.	<i>ibid</i>
418 (kit)	further comprising means to detect a signal from said signal generating portion	See composition Claim 292 above.	
419 (kit)	further comprising means to detect a signal from said one or more chemically modified or artificially altered	Page 32, 2nd ¶ ("Other container means or series of container means may contain the elements necessary to generate the signal . . .") <i>ibid</i>	

420 (kit)	wherein the ratio of the nucleic acid sequences or segments in the second portion to the first portion of the molecular bridging entity is greater than 5.	Same as Claim 348 above.	Same as Claim 348 above.
421 (kit)	wherein the ratio is greater than 10.	Same as Claim 349 above.	Same as Claim 349 above.
422 (kit)	wherein the ratio of the signal generating portions to the nucleic acid portion in any or all of the signalling entities is greater than 1.	Same as Claim 348 above.	Same as Claim 348 above.
423 (kit)	wherein the ratio of the one or more chemically modified or artificially altered polynucleotides to the nucleic acid portion in any or all of the signalling entities is greater than 1.	Same as Claim 350 above.	Same as Claim 350 above.
424 (kit)	wherein the ratio is greater than 5.	Same as Claim 351 above.	Same as Claim 351 above.
425 (kit)	wherein the ratio is greater than 10.	Same as Claim 352 above.	Same as Claim 352 above.
426 (kit)	wherein both the ratio of the nucleic acid sequences or segments in the second portion to the first portion of the molecular bridging entity is greater than 1, and the ratio of the signal generating portions to the nucleic acid portion in any or all of the signalling entities is greater than 1.	Same as Claim 353 above.	Same as Claim 353 above.
427 (kit)	wherein both the ratio of the nucleic acid sequences or segments in the second portion to the first portion of the molecular bridging entity is greater than 1, and the ratio of the one or more chemically modified or artificially altered polynucleotides to the nucleic acid portion in any or all of the signalling entities is greater than 1.	<i>ibid.</i>	<i>ibid.</i>

428 (kit)	wherein one or both ratios are greater than 5.	Same as Claim 354 above.	Same as Claim 354 above.
429 (kit)	wherein one or both ratios are greater than 10.	Same as Claim 355 above.	Same as Claim 355 above.
430 (kit)	wherein one or both ratios are greater than 5.	Same as Claim 354 above.	Same as Claim 354 above.
431 (kit)	wherein one or both ratios are greater than 10.	Same as Claim 355 above.	Same as Claim 355 above.
432 (kit)	wherein the ratio of signalling entities to the molecular bridging entity is greater than 5.	Same as Claim 356 above.	Same as Claim 356 above.
433 (kit)	wherein the ratio is greater than 10.	Same as Claim 357 above.	Same as Claim 357 above.
434 (kit)	wherein said signal generating portion is carried in a separate container from the container carrying the signalling entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion.	Page 32, 2nd ¶ ("A second container means or series of container means may contain signalling entities . . . Other container means or series of container means may contain the elements necessary to generate the signal . . .") <i>ibid.</i>	Page 32, 2nd ¶ ("A second container means or series of container means may contain signalling entities . . . Other container means or series of container means may contain the elements necessary to generate the signal . . .") <i>ibid.</i>
435 (kit)	wherein said one or more chemically modified or artificially altered polynucleotides are carried in a separate container from the container carrying the signalling entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion.		
436 (kit)	wherein said analyte comprises a biological system.	Same as Claim 295 above.	
437 (kit)	further comprising one or more supports.	Same as Claim 359 above.	
438 (composition)	wherein said one or more chemically modified or artificially altered polynucleotides comprise one or more nucleic acid analogs.	Page 15, 1st ¶ ("By polynucleotide' is meant to include both polynucleotides, polydeoxyribonucleotides, or any poly-purine, -pyrimidine or analog and combinations thereof.")	